

PATENT COOPERATION TREATY

Ploumann & Vingtoft
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From the
 INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

338 / 200

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

To:

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Date of mailing
 (day/month/year) 20.09.2004

Applicant's or agent's file reference 32436PC01	IMPORTANT NOTIFICATION
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International application No. PCT/DK 03/00423	International filing date (day/month/year) 20.06.2003	Priority date (day/month/year) 20.06.2002
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Applicant
 ASTION DERMATOLOGY AS et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.



4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Senkel, H Tel. +49 89 2399-8071	
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INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 32436PC01	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/DK 03/00423	International filing date (day/month/year) 20.06.2003	Priority date (day/month/year) 20.06.2002
International Patent Classification (IPC) or both national classification and IPC A61K31/765		
Applicant ASTION DERMATOLOGY AS et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
- ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
- These annexes consist of a total of 7 sheets.

3. This report contains indications relating to the following items:
- I ☒ Basis of the opinion
 - II ☐ Priority
 - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - IV ☐ Lack of unity of invention
 - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - VI ☐ Certain documents cited
 - VII ☐ Certain defects in the international application
 - VIII ☐ Certain observations on the international application

Date of submission of the demand 20.01.2004	Date of completion of this report 20.09.2004
Name and mailing address of the International preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Giacobbe, S Telephone No. +49 89 2399-8463 

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/DK 03/00423

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-45 as originally filed

Claims, Numbers

1-47 received on 13.07.2004 with letter of 13.07.2004

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
 - ☐ the language of publication of the international application (under Rule 48.3(b)).
 - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:
- ☐ contained in the international application in written form.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority in written form.
 - ☐ furnished subsequently to this Authority in computer readable form.
 - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
 - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.
4. The amendments have resulted in the cancellation of:
- ☐ the description, pages:
 - ☐ the claims, Nos.:
 - ☐ the drawings, sheets:
5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/DK 03/00423**

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 18, 36-47 (IA only)

because:

☒ the said international application, or the said claims Nos. 18, 36-47 (IA only) relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the Standard.

☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-47
	No: Claims	
Inventive step (IS)	Yes: Claims	1-47
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-17, 19-35
	No: Claims	18, 36-47

2. Citations and explanations

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/DK 03/00423

1. Section I

The amended claims fulfill the requirements of Art 34(2)(b) PCT, in that they do not introduce subject-matter which was not present in the application as originally filed. In particular the double disclaimer now present in the independent claims was present in original claims 1 and 5. The value of n has furthermore been restricted to 3 (also originally disclosed and exemplified).

2. Section III

Claims 18 and 36-47 are directed to a method of treatment of the human/animal body by therapy. Such subject-matter is considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT, and therefore no opinion shall be formulated with respect to industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT). However an opinion shall be formulated with respect to novelty and inventive step based on the alleged effects of the compounds/compositions.

3. Section V

3.1 Cited Documents

The following documents (D) are referred to in this Opinion; the numbering will be adhered to in the rest of the procedure:

- D1: WO 02/05850 A (PITMY INTERNAT N V ; MEYER PETRUS JOHANNES (ZA)) 24 January 2002 (2002-01-24)
- D2: WO 01/03696 A (SCARISTA LTD ; HORROBIN DAVID F (GB); GOUAILLE CHRISTINA (SE)) 18 January 2001 (2001-01-18)
- D3: WO 96/34858 A (REDDEN PETER ; SCOTIA HOLDINGS PLC (GB); MANKU MEHAR (GB); PITT ANDREA) 7 November 1996 (1996-11-07)
- D4: PATENT ABSTRACTS OF JAPAN vol. 1997, no. 11, 28 November 1997 (1997-11-28) & JP 09 194306 A (EISAI CO LTD), 29 July 1997 (1997-07-29)
- D5: MCCARTY M F ET AL: "NIACINAMIDE THERAPY FOR OSTEOARTHRITIS - DOES IT INHIBIT NITRIC OXIDE SYNTHASE INDUCTION BY INTERLEUKIN-1 IN CHONDROCYTES?" MEDICAL HYPOTHESES, EDEN PRESS, PENRITH, US, vol. 53, no. 4, October 1999 (1999-10), pages 350-360, XP002901806 ISSN: 0306-9877
- D6: WO 01/74781 A (ASTION DEV APS ;WEIDNER MORTEN SLOTH (DK)) 11 October 2001 (2001-10-11)
- D7: WO 01/74780 A (ASTION DEV APS ;WEIDNER MORTEN SLOTH (DK)) 11

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EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/DK 03/00423

October 2001 (2001-10-11)

- D8: EP-A-0 465 423 (RES FOUND MENTAL HYGIENE) 8 January 1992 (1992-01-08)
- D9: DE 42 34 188 A (BEIERSDORF AG) 14 April 1994 (1994-04-14)
- D10: US-A-5 231 087 (THORNFELDT CARL R) 27 July 1993 (1993-07-27)
- D11: DE 43 37 711 A (BEIERSDORF AG) 11 May 1995 (1995-05-11)
- D12: EP-A-0 705 605 (BEIERSDORF AG) 10 April 1996 (1996-04-10)
- D13: US-A-4 002 775 (KABARA JON J) 11 January 1977 (1977-01-11)
- D14: EP-A-0 573 253 (UNILEVER PLC ;UNILEVER NV (NL)) 8 December 1993 (1993-12-08)
- D15: KABARA J J: "MEDIUM-CHAIN FATTY ACIDS AND ESTERS AS ANTIMICROBIAL AGENTS" COSMETIC AND DRUG PRESERVATION, XX, XX, 1984, pages 275-304, XP000989750

Unless otherwise indicated reference is hereafter made to the passages cited in the Search Report

3.2 The prior art

WO 02 05850: Pharmaceutical compositions containing ethionamide and an ester of a fatty acid with an alkanol or glycerol-polyethylene glycol. Tests were performed with isoniazid, a pyridine derivative not falling under the present structure ii).

WO 01 03696: Compositions containing vitamin B6 (pyridoxine) and eicosapentaenoic acid triglyceride in the treatment inter alia of inflammation

WO 96 34858: Use of molecules obtained by linking together a fatty acid or a fatty alcohol to nicotinic acid or pyridoxine in the treatment of inflammation and nutritional disorders. *These molecules may be considered as a type of "complex".*

JP9194306: Nicotinamide alone or in combination with a sucrose fatty acid ester has antiseptic activity

XP002901806: Nicotinamide is active in the therapy of osteoarthritis, an inflammatory disease

WO0174781: Complexes of un-substituted or substituted nicotinamide derivatives and glucosaminoglycan in the treatment of inflammation and hypersensitivity

WO0174780: Complexes of un-substituted or substituted nicotinamide derivatives and H2 histamine antagonist in the treatment of inflammation and hypersensitivity

EP0465423: Monoglycerides of fatty acids possess antibacterial properties.

DE4234188: Fatty acid esters of polyols are effective anti-mycotic agents

US5231087: Esters of fatty acids with polyols are effective against inflammatory skin diseases

DE4337711: Monoglycerides of fatty acids are active as anti-bacterial agents

EP0705605: Esters of fatty acids with alcohols and polyols are effective against superinfections

US4002775: Fatty acids and their monoesters with polyols are active antimicrobial agents. This document casts doubts on the scope of the present invention, since it clearly states that higher esters of polyols do not display any antibacterial activity

EP0573253: Esters of fatty acids with lactic acid (acting as alcohol) possess anti-bacterial properties

XP000989750: Fatty acids and their monoesters with polyols are active antimicrobial agents. This document casts doubts on the scope of the present invention, since it clearly states that higher esters of polyols do not display any antibacterial activity

3.3 Art 33(2) PCT (Novelty)

The subject-matter of the present claims meets the requirements of Article 33(2) PCT.

None of the cited documents, in particular documents D1-D3, discloses a complex of a fatty acid ester and a niacinamide derivative.

3.4 Art 33(3) PCT (Inventive step)

The subject-matter of the present claims meets the requirements of Article 33(3) PCT.

Documents D2-D4 on the one side and D5-D9 plus D11 on the other disclose that the individual components of the presently-claimed compositions are active in the treatment of inflammation and hypersensitivity and possess antibacterial activity. Although the skilled person could expect that these components together would still possess their individual properties, he would have no reason, starting from the available prior art, to expect the synergistic effect shown in the present application (cf. Example 113). In this sense even document D4 would not constitute a hint, the nature of the esters of the fatty acids being different.

3.5 Art 33(4) PCT (Industrial applicability)

As stated above, no opinion is given on the question of whether present claims 18 and

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/DK 03/00423

36-47 are industrially applicable since their patentability is *inter alia* dependent upon their formulation as well as upon national and regional laws and no unifying criteria is provided in this field by the PCT.

3.6 Certain published documents (Rule 70.10)

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO/02083058	24.10.02	19.07.01	19.07.00